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Anesthesia: Essays and Researches

Original Article

Intraoperative blood glucose levels in nondiabetic patients undergoing elective major surgery under general anaesthesia receiving different crystalloid solutions for maintenance fluid

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Abstract

Context: The study was undertaken to observe the effect of different maintenance-fluid regimen on intraoperative blood glucose levels in non-diabetic patients undergoing elective major non-cardiac surgery under general anesthesia.

Aims: To know the intraoperative blood glucose levels.

Settings and Design: Prospective randomized parallel group study.

Subjects and Methods: Two hundred non-diabetic patients (100 in each group) aged between 18 years and 60 years were enrolled for this prospective randomized parallel group study. Group A patients received Ringer's lactate solution and Group B patients received 0.45% sodium chloride with 5% dextrose and 20 mmol/L potassium chloride as maintenance fluid. Capillary blood glucose (CBG) level was measured immediately before initiation of intravenous fluid therapy and thereafter hourly till the end of surgery. If at any time intraoperative CBG was found to be more than or equal to 150 mg/dL calculated dose of human soluble insulin was given as intravenous bolus equal to the amount of CBG/100 units.

Statistical Analysis Used: For comparison of normally distributed variables independent sample *t* test was done. For rest of the data, i.e., CBG_0, CBG_4 and insulin consumption Mann-Whitney U test was employed.

Results: 63% patients in group B developed at least one episode of hyperglycemia CBG ≥ 150 mg/dL) but only 29% in the Group A did so. Insulin consumption was significantly higher in Group B than in Group A to maintain normoglycemia. The relative risk of becoming hyperglycemic in Group B patients is 2.172 (95% CI 1.544 to 3.057). Number needed to harm, i.e., hyperglycemia, in Group B is 2.941 (95% CI 2 to 5).

Conclusions: We conclude that stress induced-hyperglycemic response in patients undergoing major non-cardiac surgery is common in non-diabetic population. Maintenance-fluid therapy by

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dextrose containing solution as opposed to Ringer's lactate solution increases the incidence of hyperglycemia. To achieve normoglycemia by intravenous bolus dose of human regular insulin, significantly higher doses are required in patients receiving dextrose containing saline as maintenance fluid.

Key words: Intraoperative hyperglycemia, maintenance fluid, non-diabetic patients

INTRODUCTION

Surgeries are considered to be the combination of multiple factors including tissue damage, fasting, blood-loss, effects of medication and temperature changes from a metabolic point of view.[1] Combinations of all these factors give rise to stress response. The stress response to surgery is characterized by increased secretion of pituitary hormones and activation of the sympathetic nervous system.[2] The ultimate effect of these various endocrine changes is increased catabolic activity by increased secretion of catabolic hormones like cortisol and glucagon. The effect of these endocrine and metabolic changes ultimately leads to increased neoglucogenesis and hyperglycemia. So this stress response may be quantified by the incidence of hyperglycemia. The metabolic changes appear to be proportional to the severity of the surgical trauma with plasma cortisol and blood glucose concentration rising slightly during minor surgical procedures but significantly during major intraabdominal operations.[3] Conventionally any balanced salt solution containing sodium chloride and potassium is equally effective as maintenance fluid. But the obligatory glucose requirement of brain and red blood cells can only be met by dextrose containing solutions. In a fasting patient, if carbohydrate is not provided from extraneous source, glycogenolysis and gluconeogenesis from amino acid pools provide the necessary glucose, but accelerate protein catabolism. Dextrose prevents protein catabolism.[4]

In 1993 Obata *et al*.[5] conducted a study to assess the potential benefits of perioperative glucose administration. They measured the plasma concentrations of insulin, free fatty acids, ketone bodies, amino acids, lactate, and pyruvate in patients undergoing partial gastrectomy. The results suggested that administration of glucose stimulated insulin secretion and resulted in accumulation of the substrates such as pyruvate and alanine which were utilized readily in the body. Glucose administration is useful in suppressing catabolism during upper abdominal surgery.

Different crystalloid fluids may also alter the blood glucose levels in intraoperative period.[6] Persistent hyperglycemia in the perioperative period has been consistently shown to be associated with increased postoperative complications particularly after cardiac and vascular surgery in diabetic patients. The effect of different fluid regimen has been studied in neonates and pediatric populations.[7] Though the prevalence of perioperative hyperglycemia in non-diabetic patients undergoing cardiac surgery is very high[8] but its incidence in non-diabetic patients undergoing elective major abdominal surgery is not yet known. The present study was undertaken to observe the effect of different maintenance fluid regimen on intraoperative blood glucose levels in non-diabetic patients undergoing elective major abdominal surgery under general anesthesia.

OBJECTIVES OF THIS STUDY

The metabolic changes during surgery appear to be proportional to the severity of the surgical trauma. During surgery there is insulin resistance due to rise of levels of counter regulatory hormones like glucagon, growth hormone, cortisol and catecholamines which can be indirectly observed by the incidence of hyperglycemia. Different crystalloid fluids may also alter the blood glucose levels in intraoperative period.

Previous studies concluded that plasma insulin concentrations increased significantly in the group receiving 5% dextrose showing that the usual suppression of insulin during abdominal surgery can be overcome by a strong glycemic stimulus.

The present study was undertaken to observe the effect of different maintenance fluid regimen on intraoperative blood glucose levels of non-diabetic patients undergoing elective major non-cardiac surgery under general anesthesia. Many studies also addressed the issue of perioperative glucose supplementation.

Specific objective

- To know the intraoperative blood glucose levels in two groups of patients receiving different maintenance fluids.
- To know the incidence of intraoperative hyperglycemia capillary blood glucose (CPG) ≥150 mg/dL in patients receiving Ringer's lactate solution as maintenance fluid.
- To know the incidence of intraoperative hyperglycemia in patients receiving 0.45% sodium chloride in 5% dextrose with 20 mmol/L potassium as maintenance fluid.
- Requirement of rescue insulin therapy in each group of patients.

SUBJECTS AND METHODS

After approval from institutional ethics committee, 200 non-diabetic patients (100 in each group) of (ASA) American Society of Anaesthesiologist physical status I and II of either sex, aged between 18 years and 60 years undergoing elective major abdominal (duration of surgery > 2 h) surgery were enrolled for this prospective randomized parallel group study. The patients were temporally randomized into the two study groups. Randomization list was generated by a random number function using Microsoft Excel 2003 spreadsheet resulting in a list of 200. Group A patients received Ringer's lactate (RL) solution as maintenance fluid and Group B patients received 0.45% sodium chloride with 5% dextrose and 20 mmol/L potassium chloride, as per calculated hourly infusion rate according to their body weight. Fluid deficit arising from overnight fasting was corrected by the maintenance fluid.[4] Fifty percent of total deficit was corrected in the first hour and the remaining 50% was corrected in next 2 h. Blood loss and other plasma losses were approximately calculated from mops and suction drain bottle. These losses up to the transfusion threshold (blood loss up to 15% of body weight) were replaced volume per volume with Gelofusine® (succinylated polygelatin). We targeted a urine output of at least 1 ml/kg/h intraoperatively and urine output measured every 30 min. If urine output was found to be below desired target, 200 mL bolus of Gelofusine® was given over 10 min. We also maintained systolic blood pressure between 100 and 130 mm Hg. If at any point during surgery patients became hypotensive (SBP systolic blood pressure < 100 mm Hg), additional bolus of 200 ml Gelofusine® was administered. When the hypotension was not corrected by fluid bolus alone, 3 mg mephentermine injection was administered intravenously.

All patients were pre-medicated with 0.2 mg glycopyrrolate IV, 1 mg midazolam IV, ranitidine 50 mg IV, fentanyl 2 mcg/kg IV and ondansetron 4 mg IV 5 min prior to induction of anesthesia. Following pre-oxygenation, induction of anesthesia was done with 2 mg/kg propofol intravenously and tracheal intubation facilitated by 1 mg/kg intravenous succinylcholine. Anesthesia was maintained with 66% nitrous oxide and 1% isoflurane in 33% oxygen, on controlled ventilation. Intravenous fentanyl 0.5 mcg/kg at hourly intervals was administered for intraoperative analgesia. Muscle relaxation was maintained with initial dose intravenous atracurium 0.3 mg/kg followed by 0.1 mg/kg at 30 min intervals or as clinically judged.

All patients had baseline capillary blood glucose (CBG) measured immediately prior to the start of intravenous infusion of any fluid. Thereafter, CBG levels were measured hourly till the end of surgery. Glucose concentration was determined in fresh capillary blood by reflectance photometry using an Accu-Check® active blood glucose monitor (Roche Diagnostics, Mannheim, Germany; Unit of measure: Mg/dL, measuring range: 10-600 mg/dL or 0.56-33.6 mmol/L). If at any time during the study, CBG was found to be more than or equal to 150 mg/dL, calculated dose of human soluble insulin (=CBG/100 units) was given as IV bolus.[9]

We considered CBG value of 150 mg/dL as treatment initiating point because a recent analysis of the cohort found a positive correlation between the average postoperative glucose level and mortality, with the lowest mortality in patients with average postoperative blood glucose of 150 mg/dL (8.3 mmol/L).[10]

We tested all data set of this study for normality using Shapiro-Wilk Tests of Normality. Age, weight, height, (FBS) fasting blood sugar, (PPBS) post prandial blood sugar, CBG_1, CBG_2, CBG_3, CBG_5 and duration of surgery are normally distributed ($P > 0.05$). For comparison of these variables independent sample t test was done. For rest of the data, i.e., CBG_0, CBG_4 and insulin consumption Mann-Whitney U test was employed.

RESULTS

Two hundred non-diabetic patients (100 in each group) of ASA physical status I and II of either sex, aged between 18 years and 60 years were enrolled for this prospective randomized parallel group study.

It was seen that there was no statistically significant difference between the groups in terms of the demographic characteristics of the patients namely age, height, weight, sex and ASA physical status distribution and duration of surgery. There was statistically no significant difference in FBS, PPBS and baseline CBG values between two groups [Table 1].

CBG values at 1h, 2h and 3h are significantly higher in group B than group A. But there is no significant difference between 4th h and 5th h CBG values between the groups [Table 2, Figure 1].

Insulin consumption is significantly higher in group B than group A [Table 3, Figure 2]. The difference in median insulin requirement in the two groups to maintain normoglycemia is 1.5 unit (95% CI = 1.45 unit to 1.55 unit).

29 patients out of 100 in the group A and 63 patients out of 100 in the group B developed at least one episode of hyperglycemia (CBG ≥ 150 mg/dL) during surgery. The relative risk of becoming hyperglycemic in group B patients is 2.172 (95% CI 1.544 to 3.057). Number needed to harm, i.e., hyperglycemia, in group B is 2.941 (95% CI 2 to 5). As we treated hyperglycemic episodes with intravenous bolus dosage of insulin, each new episode of hyperglycemic events was taken into account during calculation of incidence of hyperglycemia.

The incidence of hyperglycemic episode was 10.6% in group A patients and 24.5% in group B patients and the difference is statistically significant [Figure 3].

We found that CBG level increases with progression of surgery and the mean CBG values at 1st, 2nd and 3rd h are significantly higher in patients those who are receiving 0.45% sodium chloride with 5% dextrose and 20 mmol/L potassium chloride as maintenance fluid in contrast to those receiving RL solution. Exogenous insulin requirement to maintain normoglycemia is significantly higher in patients receiving dextrose containing solution is also significantly higher than those receiving RL solution. Percentage of hyperglycemic episodes in group B patients is also significantly higher than group A patients.

DISCUSSION

The present study was undertaken to observe the effect of different maintenance fluid regimen on intraoperative blood glucose levels in non-diabetic patients undergoing elective major abdominal surgery under general anesthesia. None of the previous studies was particular about their intraoperative fluid protocol.

In this study, we found that CBG level increases with progression of surgery irrespective of maintenance fluid regimen and the mean CBG values at 1st, 2nd and 3rd h are significantly higher in patients those who are receiving 0.45% sodium chloride with 5% dextrose and 20 mmol/L potassium chloride as maintenance fluid in contrast to those receiving RL solution. Exogenous insulin

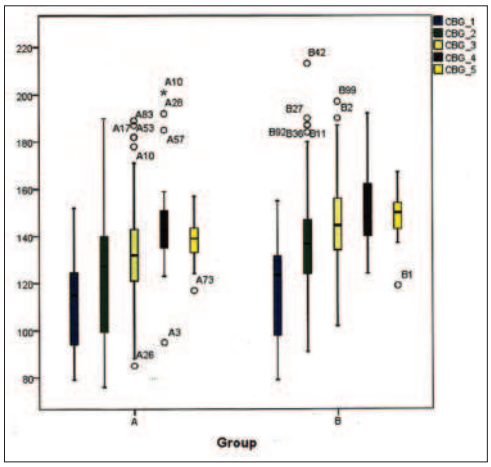

Figure 1: Distribution of capillary blood glucose_1, capillary blood glucose_2, capillary blood glucose_3, capillary blood glucose_4 and capillary blood glucose_5 respectively in two groups

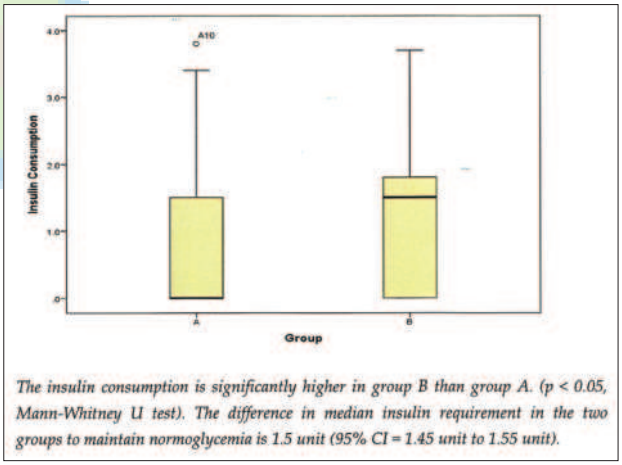

Figure 2: Comparison of insulin consumption between two groups

Table 1: Demographic and baseline clinical profile

Variables	Group A Mean±SD	Group B Mean±SD	*P* value
Age (years)	46.02±8.07	45.23±7.72	*P*>0.05$
Height (cm)	162.50±6.34	163.94±5.93	*P*>0.05$
Weight (kg)	54.77±8.05	55.60±7.78	*P*>0.05$
Duration of surgery (min)	202.90±57.41	209.75±56.78	*P*>0.05$
FBS (mg/dL)	75.65±6.39	76.71±5.34	*P*>0.05$
PPBS (mg/dL)	90.53±7.93	91.95±6.61	*P*>0.05$
CBG_0 (mg/dL)	84.02±12.27	82.03±11.79	*P*>0.05#
Sex: Male/female	57/43	57/43	*P*>0.05&
ASA PS: I/II	72/28	75/25	*P*>0.05&

$Independent sample *t*-test; #Mann-whitney U test; &Chi-square test;
ASA: PS = American society of anaesthesiologist physical status

Table 2: Group statistics for capillary blood glucose_1, capillary blood glucose_2, capillary blood glucose_3, capillary blood glucose_4 and capillary blood glucose_5

CBG	Statistic				Sig (2 tailed)	95% confidence interval of the difference	
	Group A		Group B				
	Mean±SD	Median	Mean±SD	Median		Upper	Lower
CBG_1	109.87±18.28	115.00	117.88±18.48	123.50	0.002	−13.137	−2.883
CBG_2	123.17±24.46	127.50	137.30±21.27	137.00	<0.001	−20.521	−7.739
CBG_3	132.16±22.81	132.00	145.66±19.41	144.50	<0.001	−19.998	−6.451
CBG_4	145.18±21.27	142.50	151.48±17.81	148.00	0.103 (mann-whitney U test)	Not applicable for non-normally distributed data	
CBG_5	138.0±11.18	139.00	147.45±12.44	150.00	0.075	−19.973	1.064

CBG = Capillary blood glucose; capillary blood glucose values at 1 h, 2 h and 3 h are significantly higher in group B than group A. But there is no significant difference between 4th h and 5th h capillary blood glucose values between the group [Table 2, Figure 1]

requirement to maintain normoglycemia is significantly higher in patients receiving dextrose containing solution is also significantly higher than those receiving RL solution. Percentage of hyperglycemic episodes in group B patients is also significantly higher than group A patients.

In 1983 Walsh *et al.*[11] studied effects of infusion of 0.9% sodium chloride solution, Hartmann's and 5% dextrose solution on the concentrations of circulating metabolites and insulin in patients undergoing cholecystectomy. They concluded that Hartmann's solution had a similar effect on the metabolic response to 0.9% sodium chloride solution, but the use of 5% dextrose at the rate of 5 mg/kg/min was associated with an exacerbation of the hyperglycemic response to surgery. Plasma insulin concentrations increased significantly in the group receiving 5% dextrose showing that the usual suppression of insulin during abdominal surgery can be overcome by a strong glycemic stimulus.

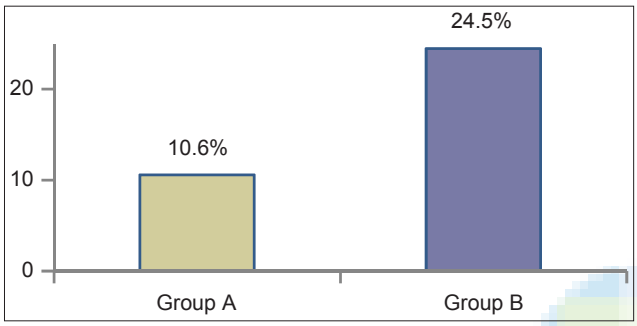

Figure 3: Incidence of hyperglycemic episodes in each group

Table 3: Comparison of insulin consumption between two groups

	Group	Statistic	Standard error	Asymp. sig. (2-tailed (mann-whitney *U*)
Insulin consumption (unit)	A			
	Mean±SD	0.51±0.85	0.0853	<0.001
	Median	0.00		
	B			
	Mean±SD	1.31±1.18	0.1180	
	Median	1.500		

Chin *et al.*[12] concluded that initiation of intravenous fluid replacement with dextrose containing solutions is not required to prevent hypoglycemia in elective surgery; however glucose administration is useful in suppressing catabolism during upper abdominal surgery.[5] Coupled with the metabolic response to surgical stress, intravenous dextrose infusion may in fact cause significant hyperglycemia. In 2008 Rasoul Azarfarin and Azin Alizahed Asl[13] concluded that the prevalence of severe hyperglycemia was high during (CABG) coronary artery bypass graft operation. In that study, prevalence of at least one episode of hyperglycemia (blood glucose > 126 mg/dL) was 95% and prevalence of severe hyperglycemia (blood glucose > 180 mg/dL) was 54.6%. However, they did not mention their intraoperative fluid protocol. Saringcarinkul and Kotrawera[14] found a progressive increase in the blood glucose values in patients receiving 5% dextrose during surgery. They defined hyperglycemia as blood glucose greater 180 mg/dL and they excluded major surgical cases. But no patient had blood glucose values more than 180 mg/dL at any point of time. On the contrary, we have included only major surgical cases in our study. Smith *et al.*[15] found that hyperglycemia (blood glucose > 144 mg/dL) occurs in 73% nondiabetic patients following renal transplant. Prasad *et al.*[16] reported that blood glucose ≥ 200 mg/dL was observed at least once in the perioperative period in 70% non-diabetic patients undergoing CABG surgery. The findings from the previous studies has been summarized in Table 4. Our observations are also corroborative with these studies.

In our study at least one episode of hyperglycemia (CBG ≥ 150 mg/dl) was observed in 29% patients receiving RL as maintenance fluid as opposed to 63% patients receiving 0.45% sodium chloride with

Table 4: Comparison of various studies on intraoperative hyperglycemia in nondiabetic population

Author	Year	Surgery	Definition of hyperglycemia	IV fluid protocol	Incidence of hyperglycemia
Azarfarin, *et al.*	2008	CABG	Hyperglycemia=BG>126 mg/dL severe hyperglycemia=BG>180 mg/dL	Not mentioned	Hyperglycemia=95% severe hyperglycemia=54.6%
Saringcarinkul, *et al.*	2009	Excluding major surgery	BG>180 mg/dL	5% dextrose	No patient was hyperglycemic
Smith, *et al.*	2005	Cardiac surgery following renal transplant	BG>144 mg/dL	Not known	73%
Prasad, *et al.*	2007	CABG	BG>200 mg/dL	Not known	70%
Our study	2012	Major non cardiac surgery	BG>150 mg/dL	Group A: Maintenance fluid RL+replacement fluid gelofusine® Group B: Maintenance fluid 0.45% NaCl with 5% dextrose and 20 mmol/L KCl+replacement fluid gelofusine	Group A: 29% Group B: 63%

CABG = Coronary artery bypass grafting; BG = Blood glucose; RL = Ringer's lactate

5% dextrose and 20 mmol/L potassium chloride as maintenance fluid. We also found that requirement of rescue insulin to maintain glycemic homeostasis in patients receiving dextrose as maintenance fluid during surgery was significantly higher than those who received RL.

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